Remarks

Claims 1-4, 13-17, 31, 33, 36-38, 45, 46, 51, 52, 57, 58 and 77 are pending in the application. In a phone conversation with Examiner Owens on September 19, 2005, she agreed to reinstate the restriction requirement with respect to the method and combination claims (Groups V, VI and VII). Accordingly, Applicant hereby withdraws the request for rejoinder. Claims 59-76 have been cancelled as being directed to non-elected subject matter. Applicant reserves the right to file a divisional application to the subject matter of the cancelled claims.

Basis for the addition of new Claims 78, 79 and 80 may be found in the originally filed claims and page 5, line 3 –8, line of the specification.

§102 Rejections

*I. Claims 1,4,13, 31, and 33 were rejected under 35 USC §102(b) as being anticipated by Duplantier (CA: 129:49198 – Duplantier, et al., J. Med Chem **41**, 2268-2277 (1998)).*

Applicant respectfully submits that the amendment of Claim 1 renders the rejection moot. Applicant reserves the right to file a continuation application directed to the cancelled subject matter.

II. Claims 1, 4, 13, 31 and 33 were rejected under 35 USC §102(b) as being anticipated by Ciba (CA 65:12344 – NL 6511645 (equivalent to US Patent Nos. 3,340,269 and 3,365,459).

Applicant respectfully submits that the amendment of Claim 1 renders the rejection moot. Applicant reserves the right to file a continuation application directed to the cancelled subject matter.

III. Claims 1, 4, 13, 31 and 33 were rejected under 35 USC §102(b) as being anticipated by Duplantier (CA 122:239696 – WO 95/01980).

Applicant respectfully submits that the amendment of Claim 1 renders the rejection moot. Applicant reserves the right to file a continuation application directed to the cancelled subject matter.

§112 Rejections

I. Claims 1-4, 13-17, 31, 33, 36-38, 45, 46, 51, 52, 57, 58, 62-77 were rejected under 35 USC §112, 1st paragraph.

Firstly, the rejection with respect to Claims 62-76 is moot since these claims have been cancelled for being directed to non-elected subject matter. Applicant reserves the right

to pursue the cancelled claims in a divisional application whereupon Applicant will address any outstanding rejections on the merits.

The only claims remaining in the application are "compound" claims. Examiner states that the nature of the invention is "the method for treating a disease, condition or disorder modulated by a cannabinoid receptor antagonist..." This is not entirely correct since most of the claims were directed to compounds and not methods of use. Combining the 112 arguments for compounds with the method claims is contrary to established law as explained below.

Applicant would also like to bring to the Examiner's attention that controlling precedent requires that the USPTO accept the objective truth of Applicant's teachings of enablement unless there is a reason to doubt these teachings. Applicant respectfully submits that there is no reason to doubt the objective truth of the statements contained within the Specification upon which Applicant relies for enabling support of his compounds.

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing the defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for the enabling support. In Re Marzocchi, 439 F.2d 220,222 (CCPA 1971).

The burden is on the Examiner to come forward with *evidence* as to why assertions of utility should not be accepted. In the instant case, the Examiner asserts that the exact role of the cannabinoid receptor is still under investigation and cites Barth, et al. which was published in 1999 (6 years old). Since this publication much has been learned about cannabinoid antagonists as evidenced by the two review articles submitted with the Supplemental Information Disclosure Statement filed on September 22, 2005. See, Smith, et al., "Recent advances in the research and development of CB1 antagonists" IDrugs, **8**(1), 53-56 (2005); Muccioli, G.G., et al, "Current Knowledge on the Antagonists and Inverse Agonists of Cannabinoid Receptors" Current Medicinal Chemistry, **12**, 1361-1394 (2005); and references cited therein, as well as the numerous references cited by Applicant in the earlier submitted Information Disclosure Statements. Clearly, compounds that bind to the cannabinoid-1 receptor have pharmacological utility, in particular, for use in treating obesity and associated metabolic disorders.

Examiner queries which receptor Applicant's compounds modulate. Applicant would like to point out to the Examiner the numerous references within the specification to the CB-1 receptor. Not only does the Applicant point out the particular receptor, but also the fact that the compounds act as a CB-1 receptor antagonist.

> "The present invention provides compounds of Formula (I) or (II) that act as cannabinoid receptor ligands (in particular, CB1 receptor antagonists)" emphasis added. See, the page 3, lines 17-18.

> "Compounds of the present invention have been shown to be useful cannabinoid receptor ligands (in particular, CB1 receptor antagonists). emphasis added. See, the page 8, lines 13-14.

> "The present invention further provides a method of treating diseases, conditions and/or disorders modulated by cannabinoid receptor antagonists in an animal that includes administering to an animal in need of such treatment a therapeutically effective amount of a compound of the present invention or a pharmaceutical composition comprising an effective amount of a compound of the present invention and a pharmaceutically acceptable excipient, diluent, or carrier. The method is particularly useful for treating diseases, conditions and/or disorders modulated by cannabinoid receptor (in particular, CB1 receptor) antagonists. emphasis added. See, the page 32, lines 15-22.

More importantly, the pharmacological data section provides evidence that the compounds of the present invention bind to the CB-1 receptor. It does not matter which disorder, condition or disease is being treated to show utility of a compound so long as there exists a disorder, condition or disease that is mediated by binding to that particular receptor. The literature evidences more than sufficient uses for compounds that bind to the cannabinoid receptors (in particular, the CB-1 receptor). As stated by Applicant in the specification, all of the compounds listed in the Example section were tested in the CB-1 receptor binding assay. The compounds provided a range of binding activities from 0.6 nM – 2500 nM (nano-molar). See, page 76, lines 6-8 of the specification.

Although Examiner acknowledged the assays beginning at page 75, she failed to see the significance of such assays. Applicant clearly stated that the binding assays were designed to detect compounds that inhibit the binding of [^{3}H] SR141716A (a known selective radiolabeled CB-1 ligand) and [^{3}H] 5-(1,1-dimethylheptyl)-2-[5-hydroxy-2-(3-hydroxypropyl)-cyclohexyl]-phenol; a known radiolabeled CB-1/CB-2 ligand) to their respective receptors.

See page 76, lines 20-23. Applicant also provided references which describe the significance of the binding assays.

> "Bioassay systems for determining the CB-1 and CB-2 binding properties and pharmacological activity of cannabinoid receptor ligands are described by Roger G. Pertwee in "Pharmacology of Cannabinoid Receptor Ligands" Current Medicinal Chemistry, 6, 635-664 (1999) and in WO 92/02640 (U.S. Application No. 07/564,075 filed August 8, 1990, incorporated herein by reference)." Page 87, lines 18-23

After each of the headings of the *in vivo* assays, a brief description is provided which outlines the utility of the test. For example, for food intake, "the following screen was used to evaluate the efficacy of test compounds for inhibiting food intake in Sprague-Dawley rats after an overnight fast". This is a standard test for evaluating compounds for use in treating obesity or weight-control.

Examiner states that the absence of evidence of functional treatment (i.e., no correlation to treatment in humans) lacks enablement. She goes on to assert that "Applicant's assertions either that the compounds would be effective or that the compounds are effective are not enough." Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an immediate benefit to the public and thus satisfies the utility requirement. *Nelson v. Bowley*, 626 F.2d 853, 206 USPQ 881 (1980). Similarly, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition.

> "We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshall resources and direct the expenditure of effort in further in vivo testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility." Cross v. Iizuka, 753 F.2d 1040, 1051, 224 USPQ 739, 739, 747-48 (Fed. Cir. 1985).

Clearly, Examiner's statements are contrary to existing law. Applicants have provided extensive descriptions of biological assays used to evaluate and predict the utility of the compounds of the present invention. In addition, the range of binding data observed for the compounds exemplified in the Examples are included on page 76, lines 6-8 which clearly

indicate the binding affinity of the compounds to the CB-1 receptor. As pointed out in the specification on page 76, lines 20-23, Applicant compared the compounds of the present invention with SR141716 (a known CB-1 antagonist) to determine binding affinity for the CB-1 receptor. The numerous references submitted through the Information Disclosure Statements provide more than ample evidence that a correlation exists between therapeutic indications and compounds that bind to the CB-1 receptor. SR141716A (also known under the tradename Acomplia™ or the generic name rimonabant) is currently before the FDA for approval for use in treating obesity and related metabolic disorders. Clearly, a nexus exists between compounds that act as CB-1 antagonists and its therapeutic use. Examiner has provided no current evidence to the contrary.

II. Claims 68 and 72 were rejected under 35 USC §112, 1st paragraph, as failing to comply with the enablement requirement.

Applicant respectfully submits that the cancellation of Claims 68 and 72 (non-elected subject matter) renders this rejection moot with respect to this application. Applicant reserves the right to pursue the cancelled claims in a divisional application whereupon Applicant will address any outstanding rejections on the merits.

III. Claims 62-72 were rejected under 35 USC §112, 1st paragraph as failing to comply with the enablement requirement.

Applicant respectfully submits that the cancellation of Claims 62-72 (non-elected subject matter) renders this rejection moot with respect to this application. Applicant reserves the right to pursue the cancelled claims in a divisional application whereupon Applicant will address any outstanding rejections on the merits.

IV. Claims 62-76 were rejected under 35 USC §112, 1st paragraph, as fialing to comply with the written description requirement.

Applicant respectfully submits that the cancellation of Claims 62-72 (non-elected subject matter) renders this rejection moot with respect to this application. Applicant reserves the right to pursue the cancelled claims in a divisional application whereupon Applicant will address any outstanding rejections on the merits.

V. Claims 63, 64, 69, 70, 73 and 74 were rejected under 35 USC §112, 2nd paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant respectfully submits that the cancellation of Claims 63, 64, 69, 70, 73 and 74 (non-elected subject matter) renders this rejection moot with respect to this application. Applicant reserves the right to pursue the cancelled claims in a divisional application whereupon Applicant will address any outstanding rejections on the merits.

§101 Rejections

I. Claims 68 and 72 were rejected under 35 USC §101 as lacking utility.

Applicant respectfully submits that the cancellation of Claims 68 and 72 (non-elected subject matter) renders this rejection moot with respect to this application. Applicant reserves the right to pursue the cancelled claims in a divisional application whereupon Applicant will address any outstanding rejections on the merits.

Based on the foregoing arguments and the amendments to the claims, Applicant respectfully submits that Claims 1-4, 13, 17, 33, 45, 46, 51, 52, 57, 58 and 77-80 are in condition for allowance.

Respectfully Submitted:

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